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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: JANE ZARA Examiner #: 77512 Date: 5/24/03
Art Unit: 1635 Phone Number 30 6-5820 Serial Number: 09/982,892
Mail Box and Bldg/Room Location: 11D03 Results Format Preferred (circle): PAPER DISK E-MAIL
1/e12

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Bioconjugate + Bio Delivery Agent

Inventors (please provide full names): Gruosso et al

Earliest Priority Filing Date: 8/22/97

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please see Attached Structure + highlighted claims.

POINT OF CONTACT:
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TECHNICAL INFO. SPECIALIST
CM1 6B06 TEL. (703) 305-1954

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	NA Sequence (#)		STN	466.34
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Date Completed:	5/28/03		Lexis/Nexis	
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PTO-1590 (8-01)

10/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12574844 BIOSIS NO.: 200000328346
Biodistribution of radiolabeled adenosylcobalamin in patients diagnosed with various malignancies.
AUTHOR: Collins Douglas A(a); Hogenkamp Harry P C; O'Connor Michael K; Naylor Stephen; Benson Linda M; Hardyman Timothy J; Thorson Linda M
AUTHOR ADDRESS: (a)Section of Nuclear Medicine, Mayo Clinic, 200 First St SW, Rochester, MN, 55905**USA
JOURNAL: Mayo Clinic Proceedings 75 (6):p568-580 June, 2000
MEDIUM: print
ISSN: 0025-6196
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: cntdot Objective: To study the biodistribution of a *vitamin* *B12* analog, indium In 111-labeled diethylenetriaminepentaacetate adenosylcobalamin (In 111 DAC), in patients recently diagnosed as having primary or recurrent malignancy. cntdot Patients and Methods: Thirty...

...system malignancies were studied prior to definitive surgery or biopsy. A maximum of 650 muCi (2.2 mug) of In 111 DAC was administered intravenously. *Vitamin* *B12* and folate levels were determined prior to injection. Serum clearance and urinary and stool excretion of the tracer were measured. Images were routinely obtained at...

...was 7 minutes. Average urinary and stool excretion of the injected dose over 24 hours was 26.1% and 0.4%, respectively. The greatest focal *uptake* of In 111 DAC occurred in the liver and spleen, followed by the nasal cavity and salivary and lacrimal glands. The average tumor *uptake* of the injected dose was 2% at 30 minutes and 1.5% at 24 hours. High-grade primary and metastatic breast, lung, colon, thyroid, and...

...nonpalpable breast cancers were delineated by In 111 DAC. Low-grade malignancies as well as early skeletal metastatic disease were not effectively imaged by the *vitamin* *B12* tracer. Patients with elevated baseline *vitamin* *B12* or those concurrently taking corticosteroids appeared to have optimal visualization of their malignancies. cntdot Conclusion: *Vitamin* *B12* may be a useful vehicle for *delivering* diagnostic and therapeutic agents to various malignancies. Further evaluation of cobalamin analogs and their interaction with transport proteins and *cellular* receptors within malignant tissue and infection is warranted.

10/3,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12315582 BIOSIS NO.: 200000073449
Synthesis and biological activity of ribose-5'-carbamate derivatives of vitamin B12.
AUTHOR: McEwan J F(a); Veitch H S; Russell-Jones G J
AUTHOR ADDRESS: (a)Biotech Australia Pty Ltd., Roseville, NSW**Australia
JOURNAL: Bioconjugate Chemistry 10 (6):p1131-1136 Nov.-Dec., 1999
ISSN: 1043-1802
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Twelve biologically active derivatives of *vitamin* *B12* (cyanocobalamin) have been synthesized in which spacers were attached to

the ribose-5'-hydroxyl group of *vitamin* *B12*. Their potential to act as oral *delivery* agents for proteins, nanospheres, or immunogens using the *vitamin* *B12* *uptake* system was evaluated by determining their affinity for intrinsic factor (IF) and non-IF. The ribose-5'-hydroxyl group of *vitamin* *B12* was activated through the use of 1,1'-carbonyldiimidazole (CDI), 1,1'-carbonyldi(1,2,4-triazole) (CDT), or di(1-benzotriazolyl) carbonate (DBTC). Subsequent addition of an aminoalkane, diaminoalkane, or alkane diacid dihydrazide gave rise to *vitamin* *B12* derivatives suitable for attachment to various proteins, peptides, or nanospheres to enable oral *delivery* utilizing the *vitamin* *B12* *uptake* system. The ribose-5'-carbamate derivatives were found to possess similar affinity for intrinsic factor as that of the e-monocarboxylic acid of *vitamin* *B12*. The affinityfor non-IF was similar to cyanocobalamin or even higher for some of the smaller derivatives. Polysciences nanoparticles derivatized with *vitamin* *B12* 5'-carbamate adipic dihydrazide into CaCo-2 *cells* showed significantly higher levels of transport of the particles, when compared to unmodified particles.

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: ...*vitamin* *B12* ribose-5'-carbamate derivatives...

...analysis, biological activity, *cell* *uptake*, intrinsic factor affinity, oral *delivery* agent, synthesis

10/3,K/3 (Item 3 from file: 5)

07425915 BIOSIS NO.: 000091031904

OXIDATIVE DAMAGES AND REPAIR IN EUGLENA-GRACILIS EXPOSED TO OZONE II. MEMBRANE PERMEABILITY AND *UPTAKE* OF METABOLITES

AUTHOR: CHEVRIER N; CHUNG Y S; SARHAN F
AUTHOR ADDRESS: DEP. BIOL., UNIV. QUEBEC MONTREAL, C.P. 8888, SUCC. A, MONTREAL H3C 3P8, CAN.

JOURNAL: PLANT CELL PHYSIOL 31 (7). 1990. 987-992. 1990
FULL JOURNAL NAME: Plant and Cell Physiology
CODEN: PCPHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

OXIDATIVE DAMAGES AND REPAIR IN EUGLENA-GRACILIS EXPOSED TO OZONE II. MEMBRANE PERMEABILITY AND *UPTAKE* OF METABOLITES

ABSTRACT: Significant injuries to the plasma membrane were detected in Euglena gracilis *cells* during ozone exposure (240 .mu.l .cntdot.liter-1, *delivery* rate of 1 .mu.mol .cntdot. min-1), as assessed by measuring the alterations of *vitamin* *B12* and acetate uptakes and the leakage of intracellular K+ (Rb+). A rapid decrease in the *uptake* of *vitamin* *B12* and acetate was observed within 15 min of treatment, indicating that both transport systems are very sensitive to O3. On the other hand, the leakage of intracellular K+ ions, as measured by the efflux of 86Rb+ from prelabelled *cells*, could only be detected after 30 min of O3 exposure. These results suggest that the initial metabolic symptoms of injury is at the level of...

...of the membrane permeability to K+ ions appears as a second step in the cascade of oxidative events at the plasma membrane level. When Euglena *cells* were allowed to recover under autotrophic growth conditions following O3 treatment, *vitamin* *B12* and 86Rb+ (K+) ions uptakes returned gradually to control level within 5 h of the recovery period. Acetate *uptake* returned to control level at a slower rate and needed 20 h for complete recovery. These results indicate that the *cells* were able to actively repair most of the initial oxidative damages induced by O3. The metabolic significance of the repair mechanism(s) is discussed.

DESCRIPTORS: INTRACELLULAR POTASSIUM ION LEAKAGE ACETATE *UPTAKE* VITAMIN

B-12 *UPTAKE* TRANSPORT SYSTEM METABOLISM CELL INJURY AIR POLLUTION

10/3,K/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02453149 BIOSIS NO.: 000066035693
THE LYMPHOCYTE AS A MARKER OF PAST NUTRITIONAL STATUS PERSISTENCE OF ABNORMAL LYMPHOCYTE DEOXY URIDINE SUPPRESSION TEST AND CHROMOSOMES IN PATIENTS WITH PAST DEFICIENCY OF FOLATE AND VITAMIN B-12
AUTHOR: DAS K C; HERBERT V
AUTHOR ADDRESS: 130 W. KINGSBRIDGE RD., BRONX, N.Y. 10468, USA.
JOURNAL: BR J HAEMATOL 38 (2). 1978 219-234. 1978
FULL JOURNAL NAME: British Journal of Haematology
CODEN: BJHEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In short-term suspension cultures of bone marrow *cells* of PHA[phytohemagglutinin]-stimulated lymphocytes from normal subjects, non-radioactive deoxyuridine (dU) suppressed the incorporation of radioactive thymidine ([3H]TdR) or its analogue, [125I]deoxyuridine ([125I]UdR), into DNA. This normal suppression by deoxyuridine (dU) was impaired in both of these *cell* systems from patients with deficiency of folate or *vitamin* *B12*, and corrected by the appropriate vitamin. Patients with megaloblastic anemia due to deficiency of *vitamin* *B12* or folate were studied before and after treatment. When treatment returned to normal the bone marrow morphology and the serum and red *cell* vitamin levels, then the dU suppression test and chromosomal changes in the bone marrow were also corrected. The dU suppression test and chromosomal changes remained...

...long as 84 d after therapy. These abnormal lymphocyte dU suppression tests were corrected by the appropriate in vitro additions of folid acid, methylfolate and *vitamin* *B12*, depending on the vitamin deficiency present before therapy. Apparently an abnormal lymphocyte dU suppression test corrected by the appropriate vitamin in vitro, and characteristic chromosome abnormalities in lymphocytes, when these are absent in the bone marrow, indicate past deficiency of *vitamin* *B12* or folate. These changes can be used for retrospective diagnosis of these deficiencies in patients treated by shotgun therapy. Apparently circulating unstimulated lymphocytes: do not incorporate appreciable amounts of *vitamin* *B12* or folic acid; reflect the vitamin status of the patient at the time the lymphocytes were generated; and cannot replace bone marrow in dU suppression tests aimed at diagnosis of current marrow and other non-lymphocyte *cell* line nutrient status. Selective nutrient deficiency may occur in one but not another *cell* line in the same person, and more studies are needed on factors affecting nutrient *delivery*, *uptake* and utilization of various human *cell* lines. These studies also provide a new approach to evaluation of circulating lymphocyte age.

10/3,K/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02139865 BIOSIS NO.: 000063054867
INHIBITION OF VITAMIN B-12 BINDING TO TRANS COBALAMIN II AT LOW PH BASIS OF A PROCEDURE FOR QUANTITATION OF CIRCULATING TRANS COBALAMIN II AND R BINDERS
AUTHOR: GILBERT H S
JOURNAL: J LAB CLIN MED 89 (1). 1977 13-24. 1977
FULL JOURNAL NAME: Journal of Laboratory and Clinical Medicine
CODEN: JLCMA
RECORD TYPE: Abstract

ABSTRACT: A diminution in the binding of exogenous *vitamin* *B12* by serum or plasma at pH 1.5 to 2 (acid-resistant binding capacity, ARBC) as compared with the binding capacity at neutral pH (unsaturated *vitamin* *B12* binding capacity, UBBC) was observed. This phenomenon was attributable to the absence of transcobalamin II (TC II)-associated *vitamin* *B12* from serum labeled at low pH, as demonstrated by gel chromatography on Sephadex G-200. Further confirmation was obtained by demonstration of a significant correlation...

...and the R binder content, quantitated as resistance to precipitation by ammonium sulfate at a 2 M concentration. Serum labeled at acid pH failed to *deliver* *vitamin* *B12* to HeLa *cells*, indicating absence of a functional TC II-B12 complex. The differing *vitamin* *B12* binding capacities of neutral and acidified material was utilized to fractionate the unsaturated *vitamin* *B12*-binding proteins of serum and plasma. The ARBC was used to measure the R binder content, and TC II was calculated from the difference between...

...fractionation procedure was performed on 75 sera and showed increased ARBC in patients with myeloproliferative disorders and decreased ARBC in leukopenia. The content of unsaturated *vitamin* *B12*-binding protein was compared in 75 paired samples of serum and plasma collected from EDTA-anticoagulated blood containing NaF to inhibit release of granulocyte binders...

...of fluoridated plasma was significantly lower, due to decreased in vitro R binder release. Plasma also contained less TC II, possibly related to in vitro *cellular* *uptake* of this binder in fluoridated plasma.

10/3,K/6 (Item 1 from file: 135)
DIALOG(R)File 135:NewsRx Weekly Reports

0000069182 (USE FORMAT 7 OR 9 FOR FULLTEXT)
Vitamin-mediated tumor targeting data confirm enhanced drug *uptake*
Biotech Week, November 6, 2002, p.17

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English
RECORD TYPE: FULLTEXT
WORD COUNT: 528

Vitamin-mediated tumor targeting data confirm enhanced drug *uptake*

...TEXT: vitro and in vivo data on vitamin targeted polymers.

Linking drugs to polymers increases the circulation time of cancer drugs and results in increased tumor *uptake* due to the enhanced permeability and retention (EPR) effect as a result of the "leaky" blood vessels at a tumor site. Access has combined the advantages of polymers with the knowledge that many aggressive tumors overexpress surface receptors involved in the *uptake* of vitamin B12 and folate.

... advantages due to greater specificity of delivery. A challenge to this approach is to identify markers that are overexpressed on the surface of numerous tumor *cell* types but not on normal *cells*. Many aggressive tumors overexpress surface receptors involved in the *uptake* of *vitamin* *B12* and/or folate, which has been demonstrated through the ability to differentiate between malignant and benign tumors using imaging techniques such as radiopharmaceuticals.

The company...

...and was further enhanced with vitamin B12 or folate.

The data demonstrate that vitamin-targeted polymers have the potential to greatly increase the level of *uptake* of cancer therapeutics into tumor cells. This represents a potentially exciting development in tumor-targeting and therapy, according to Access.

Data also were presented from in vitro studies of several tumor cell lines, known to overexpress receptors involved in the *uptake* of vitamin

B12 and/or folate to evaluate the ability to internalize the targeted HPMA polymer. Vitamin-mediated *uptake* was observed. For example, a tumor cell line that is known to overexpress folate receptors exhibited a sixfold increased *uptake* of the folate targeted HPMA and in another tumor cell line an eightfold higher level of *uptake* was seen with the vitamin B12 targeted polymer.

Commenting on the vitamin-mediated tumor-targeting posters, Kerry P. Gray of Access stated, "This is a...

...to improve cancer therapy. These data, combined with previous preclinical studies, clearly indicate that vitamin B12 and folate can be utilized successfully to increase tumor *uptake* and achieve improved tumor inhibition."

Internal research programs are focused on identifying a preclinical development candidate during the upcoming 12 months using the vitamin-mediated targeting technology.

Gray continued, "Cancer is our initial focus with the vitamin-mediated targeting technology. However, overexpression of receptors involved in the *uptake* of vitamin B12 and/or folate occur in other diseases including rheumatoid arthritis, Crohn's disease, ulcerative colitis, and autoimmune disorders. Consequently, this technology has...

10/3,K/7 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10490408 96300913 PMID: 8708525
Serum transcobalamin II level in glucose-6-phosphate dehydrogenase deficient subjects with typhoid fever.
Areekul S; Paksanond S; Thanomsak W; Vatanavicharn S
Department of Tropical Radioisotopes, Faculty of Tropical Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.
Journal of the Medical Association of Thailand = Chotmaihet thangphaet (THAILAND) May 1996, 79 (5) p325-9, ISSN 0125-2208 Journal Code: 7507216
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Transcobalamin II (TCII) is the *vitamin* *B12* binding protein which is responsible for *delivery* of this vitamin to the tissues. High values for serum TCII have been reported in many clinical conditions. This paper describes the elevated serum TCII...

... serum TCII during hemolysis is probably due to hemoglobinuria secondary to excessive hemolysis. As Hb is known to be efficiently reabsorbed by the proximal tubule *cells* and can competitively inhibit the tubular *uptake* of TCII-B12. It is possible that excess Hb interferes with TCII *uptake* and degradation at renal tubular *cells*. Therefore, the circulating TCII survival is prolonged resulting in the elevated TCII level. Furthermore, lysosomal degradation of newly synthesized TCII is a normal process that regulates the TCII secretion. Therefore, a reduced lysosome-mediated *uptake* of TCII-B12 by renal tubular *cell* may stimulate the TCII secretion as has been shown experimentally in vitro.

10/3,K/8 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02385023 77072952 PMID: 12239
Inhibition of vitamin B12 binding to transcobalamin II at low pH: basis of a procedure for quantitation of circulating TC II and R binders.
Gilbert H S
Journal of laboratory and clinical medicine (UNITED STATES) Jan 1977,

89 (1) p13-24, ISSN 0022-2143 Journal Code: 0375375
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A diminution in the binding of exogenous *vitamin* *B12* by serum or plasma at pH 1.5 to 2 (acid-resistant binding capacity, ARBC) as compared with the binding capacity at neutral pH (unsaturated *vitamin* *B12* binding capacity, UBBC) was observed. This phenomenon was found to be attributable to the absence of transcobalamin II (TC II)-associated *vitamin* *B12* from serum labeled at low pH, as demonstrated by gel chromatography on Sephadex G-200. Further confirmation was obtained by demonstration of a significant correlation...

... ARBC and the R binder content, quantitated as resistance to precipitation by ammonium sulfate at a 2M concentration. Serum labeled at acid pH failed to *deliver* *vitamin* *B12* to Hela *cells* indicating absence of a "functional" TC II-B12 complex. The differing *vitamin* *B12* binding capacities of neutral and acidified material was utilized to fractionate the unsaturated *vitamin* *B12*-binding proteins of serum and plasma. The ARBC was used to measure the R binder content, and TC II was calculated from the difference between...

... fractionation procedure was performed on 75 sera and showed increased ARBC in patients with myeloproliferative disorders and decreased ARBC in leukopenia. The content of unsaturated *vitamin* *B12*-binding protein was compared in 75 paired samples of serum and plasma collected from EDTA-anticoagulated blood containing sodium fluoride to inhibit release of granulocyte...

...of fluoridated plasma was significantly lower, due to decreased in vitro R binder release. Plasma also contained less TC II, possibly related to in vitro *cellular* *uptake* of this binder in fluoridated plasma.

10/3,K/9 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

01780432 PMID: 90660565
PLANT ALKALOIDS: THE VINCA ALKALOIDS.
Castle
Dept. of Pharmacology, Eastern Virginia Medical Sch., P.O. Box 1980, Norfolk, VA 23501
Cancer Growth Prog 1989, 10 p147-51,
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

... sites on tubulin and block the polymerization of tubulin into microtubules. This disruption of microtubule formation eventually leads to inhibition of mitosis, metaphase arrest, and *cell* death. Precise knowledge of the pharmacokinetics, distribution, metabolism, and excretion of the Vinca alkaloids has been difficult to obtain. Although vincristine and vinblastine induce a...

...marked differences in the incidence and severity of these toxic effects. There is no adequate explanation for these discrepancies, but differences in the rate of *uptake* into *cells* and the formation of toxic metabolites have been suggested. The toxicity of these Vinca alkaloids most likely results from their ability to bind to tubulin...

... primarily of supportive care and adjustment of dosage. Considerable clinical study has been devoted recently to ways of countering the neurotoxic effects of vincristine. Thiamine, *vitamin* *B12*, folinic acid,

pyridoxine, and glutamic acid all have been tried clinically, but only glutamic acid has shown any benefit. Greater success has been achieved in ...

... agents and to bolus administration of Vinca alkaloids. Another approach has been to link Vinca alkaloids to a monoclonal antibody in an attempt to increase *delivery* of the drug to the site of the tumor. The observation that calcium-channel blockers reverse the development of resistance to the Vinca alkaloids is...

10/3,K/10 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit

01073206 PMID: 77602576
THE PLASMA TRANSPORT OF VITAMIN B12.
Allen
Washington Univ. School Medicine, St. Louis, MO 63110
Br J Haematol 1976, 33 (2) p161-171, ISSN 0007-1048
Document Type: JOURNAL ARTICLE
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

The structure, function, and quantitative role of transcobalamin I (TC I), II (TC II), and III (TC III) in the plasma transport of *vitamin* *B12* are discussed. The total amounts of endogenous *vitamin* *B12* and unsaturated *vitamin* *B12* binding capacity that are actively cleared from human plasma per 24 hr, as well as the amounts mediated by or attributable to TC I, TC II, and TC III are estimated. Plasma levels alone can be extremely misleading indicators of actual *vitamin* *B12* transport as is demonstrated by the fact that TC I, which contains 70-90% of the total plasma *vitamin* *B12*, mediates less than 0.4% of the total *cellular* *uptake* of *vitamin* *B12* from plasma. This may explain why patients with congenital deficiencies of all R-type proteins and low total plasma *vitamin* *B12* levels do not have any of the signs or symptoms of actual *vitamin* *B12* deficiency. TC II contains only 10%-20% of the total plasma *vitamin* *B12*, but mediates 33%-99% of the total plasma *vitamin* *B12* clearance and greater than 99% of the plasma *vitamin* *B12* clearance that is effected by *cells* other than hepatocytes. This may explain that patients with congenital TC II deficiency have severe megaloblastic anemia despite the fact that they have normal levels of total plasma *vitamin* *B12*. Although TC III contains only 0%-10% of the total plasma *vitamin* *B12*, it may be significant in plasma *vitamin* *B12* transport and could mediate as much as 67% of the total plasma *vitamin* *B12* clearance. The fact that the hematological and neurological signs of *vitamin* *B12* deficiency are not observed in congenital R-type protein deficiency is not surprising as TC III *delivers* *vitamin* *B12* exclusively to hepatocytes. Thus other *cells*, even hepatocytes, are still able to receive *vitamin* *B12* via TC II. TC III may serve to prevent the dissemination of *vitamin* *B12* analogues throughout the body.

10/3,K/11 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals

00041778

Amyotrophic Lateral Sclerosis; Recent Advances in Pathogenesis and Therapeutic Trials (NEUROLOGICAL REVIEW)

MITSUMOTO, HIROSHI; HANSON, MAURICE R.; CHAD, DAVID A.
Archives of Neurology
February, 1988; 45: 189-2021988;

LINE COUNT: 00728 WORD COUNT: 10047

... 6) suggested that several possibilities might pertain to the pathogenesis of ALS; these include a failure in neurotrophic hormone release by muscle, a failure of *uptake* of the factor by the presynaptic motor axon terminal, and impairment in the retrograde axonal transport of the factor to the cell body. The work...patients with ALS, using a series of different analytic procedures. This group has also shown that erythrocytes from patients with ALS have more increased lead *uptake* and more fragility to mechanical stimuli than do control erythrocytes when lead is added to plasma. (Ref. 270) They believe that the increased plasma lead ...

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...intravenous MK-771 (a TRH analog) does not improve muscle strength. Muscle Nerve 1986;9:104.

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...Guamanians with amyotrophic lateral sclerosis and parkinsonism-dementia. Ann Neurol 1981;10:193-196.

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...sclerosis sera on cultured cholinergic neurons. Neurology 1983;33:317-322.

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Set	Items	Description
S1	0	(CELL (W) MEDIATED (W) ENDOCYTOSIS) (S) TOXIC?
S2	611	COBALT (S) (CELL OR CELLULAR) (S) (DELIVERY OR UPTAKE)
S3	230	RD (unique items)
S4	2	S3 AND (VITAMIN (W) B12)

>>>KWIC option is not available in file(s): 399

4/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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09763879 BIOSIS NO.: 199598218797
Effects of cobalt and vitamin B-12 on the growth of Chrysochromulina polylepis (Prymnesiophyceae).
AUTHOR: Graneli Edna(a); Risinger Lars
AUTHOR ADDRESS: (a)Ecology Bldg., Dep. Marine Ecology, S-223 62 Lund** Sweden
JOURNAL: Marine Ecology Progress Series 113 (1-2):p177-183 1994
ISSN: 0171-8630
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Atlantic sea water with a low *cobalt* (Co) concentration (0.02 nM) was enriched with Co additions (0.2, 0.5, 1.0 and 3.0 nM), inoculated with a monoculture of...

...C. polylepis was 0.8 d-1. Growth rate during the exponential phase was not influenced by Co concentrations, possibly due to Co contamination. The *cell* quota of Co for C. polylepis in the stationary growth phase was estimated at 0.55 to 0.69 fg Co *cell*-1 based on *cell* yield in relation to Co *uptake* and 0.55 to 0.70 fg Co *cell*-1 based on analysis of cells. In the 1988 C. polylepis bloom in the Kattegat and Skagerrak, *cell* concentrations reached levels of 100 times 10-6 cells l-1, requiring a Co supply of at least 1 nM. Concentrations of Co in the...
...REGISTRY NUMBERS: *VITAMIN* *B12*;
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...*VITAMIN* *B12*;

4/3,K/2 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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82122910 CA: 82(19)122910k JOURNAL
Delivery of cobalt-57-labeled B12 (vitamin B12) to lymphoblasts derived from mice with transplanted 1210 ascities tumor cell by transcobalamins I, II, III
AUTHOR(S): Meyer, Leo M.; Gams, Richard A.; Ryel, Elaine M.; Miller, Inez E.; Kumar, Sudhir
LOCATION: Hematol. Sect., VA Hosp., Brooklyn, N. Y.
JOURNAL: Proc. Soc. Exp. Biol. Med. DATE: 1974 VOLUME: 147 NUMBER: 3
PAGES: 679-80 CODEN: PSEBAA LANGUAGE: English

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S1	0	(CELL (W) MEDIATED (W) ENDOCYTOSIS) (S) TOXIC?
S2	611	COBALT (S) (CELL OR CELLULAR) (S) (DELIVERY OR UPTAKE)
S3	230	RD (unique items)
S4	2	S3 AND (VITAMIN (W) B12)
S5	374	(VITAMIN (W) B12) (S) DELIVER?
S6	127	S5 (S) CELL?
S7	68	RD (unique items)
S8	9	S7 AND (COMPLEX? OR CONJUGAT?)
S9	11	S7 AND UPTAKE
S10	11	RD (unique items)

file(s): 399

8/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13694824 BIOSIS NO.: 200200323645
The common G775C polymorphism in transcobalamin II (TC II) influences indices of vitamin B12 status in healthy older adults.
AUTHOR: Miller Joshua W(a); Ramos Marisa I(a); Garrod Marjorie G(a); Flynn Margaret A; Green Ralph(a)
AUTHOR ADDRESS: (a)Univ. of California, Davis, 4645 Second Ave., Sacramento, CA, 95817**USA
JOURNAL: FASEB Journal 16 (4):pA265-A266 March 20, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The serum protein, TC II, transports *vitamin* *B12* (B12) from the ileum to the tissues. The B12-TC II *complex* (holoTC II) is then taken up into *cells* by receptor-mediated endocytosis. A common polymorphism in TC II (G775C) has been identified in which proline replaces arginine at codon 259. Previous studies have...
...respectively; p=0.05). Our results suggest that the PP genotype has higher affinity for B12 than the AA genotype, resulting in more efficient tissue *delivery* and enhanced B12 functional status.

8/3,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11794032 BIOSIS NO.: 199900040141
Absorption of dietary and supplemental folate in women with prior pregnancies with neural tube defects and controls.
AUTHOR: Neuhouser Marian L(a); Beresford Shirley A A; Hickok Durlin E; Monsen Elaine R
AUTHOR ADDRESS: (a)Fred Hutchinson Cancer Res. Cent., 1100 Fairview Ave. N., MP-702, PO Box 19024, Seattle, WA 9810**USA
JOURNAL: Journal of the American College of Nutrition 17 (6):p625-630 Dec., 1998
ISSN: 0731-5724
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: use of dietary supplements; use of fortified foods; and/or increased intake of naturally occurring folate from foods. Identification of the most effective vehicle for *delivery* of folate to all women is critical in order to prevent these devastating congenital defects. Objective: To investigate the difference in response to an oral...

...We compared the absorption of test doses of 400 mug pteroylglutamic acid (unconjugated or synthetic folic acid found in supplements) and 400 mug pteroylpolyglutamic acid (*conjugated* or food folate) in 10 women with a history of neural tube defect affected pregnancies and eight controls with normal birth outcomes. The folate test...

...at 1, 2 and 3 hours post dose and applying a t-test to compare within and between cases and controls. We also compared red *cell* folate, *vitamin* *B12*, zinc and homocysteine between cases and controls. Results: Within group comparisons showed that the area under the curve was significantly greater for the pteroylglutamic acid...

...all women synthetic folic acid as supplements or fortified foods may be the best way to increase acute folate levels in the blood, and thus *delivery* to the developing embryo. Further, since case women had a diminished response to both forms of the vitamin, and some case women had almost no...

8/3,K/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10746426 BIOSIS NO.: 199799367571
Antibodies to transcobalamin II block in vitro proliferation of leukemic cells.
AUTHOR: McLean Gary R; Ouadros Edward V; Rothenberg Sheldon P; Morgan A Charles; Schrader John W; Ziltener Hermann J(a)
AUTHOR ADDRESS: (a)Biomed. Res. Cent., 2222 Health Science Mall, Univ. B.C., Vancouver, BC V6T 1Z3**Canada
JOURNAL: Blood 89 (1):p235-242 1997
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The plasma protein transcobalamin II (TCII) binds and *delivers* cobalamin (Cbl; *vitamin* *B12*) to all *cells*, which internalize the TCII/Cbl *complex* by receptor-mediated endocytosis. Congenital deficiency of TCII results in intracellular Cbl deficiency, one effect of which is to disrupt DNA synthesis, leading to megaloblastic anemia. We report here an in vitro culture system in which *cell* growth is dependent on *delivery* of Cbl to *cells* by TCII. Recombinant human holo-TCII was shown to support in dose-dependent manner the growth of the human erythroleukemic *cell* line K562 and the murine lymphoma *cell* line BW5147. Free Cbl also supported *cell* growth; however, at 100- to 1,000-fold higher concentrations than those effective in the presence of apo-TCII. To determine if *cellular* depletion of Cbl could be achieved by interfering with interactions between TCII/Cbl and its *cell*-surface receptor, several monoclonal antibodies raised against human TCII were studied. Three antibodies, found to compete for the same binding site on TCII, proved to be effective inhibitors of TCII/Cbl-dependent *cell* growth. Our results suggest that monoclonal anti-TCII antibodies that block the function of this protein may prove useful in antitumor therapies.

8/3,K/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02139865 BIOSIS NO.: 000063054867
INHIBITION OF VITAMIN B-12 BINDING TO TRANS COBALAMIN II AT LOW PH BASIS OF A PROCEDURE FOR QUANTITATION OF CIRCULATING TRANS COBALAMIN II AND R BINDERS
AUTHOR: GILBERT H S
JOURNAL: J LAB CLIN MED 89 (1). 1977 13-24. 1977
FULL JOURNAL NAME: Journal of Laboratory and Clinical Medicine
CODEN: JLCMA
RECORD TYPE: Abstract

ABSTRACT: A diminution in the binding of exogenous *vitamin* *B12* by serum or plasma at pH 1.5 to 2 (acid-resistant binding capacity, ARBC) as compared with the binding capacity at neutral pH (unsaturated *vitamin* *B12* binding capacity, UBBC) was observed. This phenomenon was attributable to the absence of transcobalamin II (TC II)-associated *vitamin* *B12* from serum labeled at low pH, as demonstrated by gel chromatography on Sephadex G-200. Further confirmation was obtained by demonstration of a significant correlation...

...and the R binder content, quantitated as resistance to precipitation by ammonium sulfate at a 2 M concentration. Serum labeled at acid pH failed to *deliver* *vitamin* *B12* to HeLa *cells*, indicating absence of a functional TC II-B12 *complex*. The differing *vitamin* *B12* binding capacities of neutral and acidified material was utilized to fractionate the unsaturated *vitamin* *B12*-binding proteins of serum and plasma. The ARBC was used to measure the R binder content, and TC II was calculated from the difference between...

...fractionation procedure was performed on 75 sera and showed increased ARBC in patients with myeloproliferative disorders and decreased ARBC in leukopenia. The content of unsaturated *vitamin* *B12*-binding protein was compared in 75 paired samples of serum and plasma collected from EDTA-anticoagulated blood containing NaF to inhibit release of granulocyte binders...

...of fluoridated plasma was significantly lower, due to decreased in vitro R binder release. Plasma also contained less TC II, possibly related to in vitro *cellular* uptake of this binder in fluoridated plasma.

8/3,K/5 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09834251 21644988 PMID: 11787717
Binding of transcobalamin II by human mammary epithelial cells.
Adkins Y; Lonnerdal B
Department of Nutrition, University of California, Davis 95616, USA.
Advances in experimental medicine and biology (United States) 2001, 501 p469-77, ISSN 0065-2598 Journal Code: 0121103
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

...important role during milk production and may influence the nutrient's bioavailability to the infant. Human milk and plasma contain at least two types of *vitamin* *B12* binders: transcobalamin II (TCII) and haptocorrin (Hc). *Vitamin* *B12* in milk is exclusively bound to Hc (Hc-B12). In plasma, the major *vitamin* *B12* binding protein that is responsible for *delivering* absorbed *vitamin* *B12* to most tissues and *cells* is TCII (TCII-B12). Currently, little is known about the route of secretion of *vitamin* *B12* into human milk. It is possible that a receptor-mediated pathway is involved, since maternal *vitamin* *B12* supplementation increases the amount of the vitamin secreted into human milk if the mother's *vitamin* *B12* consumption is low, but remains unchanged if her intake is adequate. In this study, we investigated the process by which the mammary gland acquires *vitamin* *B12* from maternal circulation, whether as a free vitamin or as a Hc-B12 or TCII-B12 *complex*. TCII was purified from plasma incubated with [57Co]vit B12 (B12*), while Hc was purified from whey incubated with B12*. Both proteins were separated by...

... the separated proteins was assessed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Binding studies were carried out on a monolayer of normal human mammary epithelial *cells* (HMEC) at 4 degrees C using free B12* and TCII-B12* and Hc-B12* *complexes*. Minimal binding of free B12* and Hc-B12* to HMEC was observed; however, HMEC exhibited a high affinity for the TCII-B12* *complex*. This study suggests that a specific *cell* surface receptor for the TCII-B12 *complex* exists in the mammary gland. It is possible that once *vitamin* *B12* is in the mammary gland it is transferred to Hc (which may be synthesized by the mammary gland) and then secreted into milk as a Hc-B12 *complex*.

8/3,K/6 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02385023 77072952 PMID: 12239

Inhibition of vitamin B12 binding to transcobalamin II at low pH: basis of a procedure for quantitation of circulating TC II and R binders.

Gilbert H S

Journal of laboratory and clinical medicine (UNITED STATES) Jan 1977, 89 (1) p13-24, ISSN 0022-2143 Journal Code: 0375375

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A diminution in the binding of exogenous *vitamin* *B12* by serum or plasma at pH 1.5 to 2 (acid-resistant binding capacity, ARBC) as compared with the binding capacity at neutral pH (unsaturated *vitamin* *B12* binding capacity, UBBC) was observed. This phenomenon was found to be attributable to the absence of transcobalamin II (TC II)-associated *vitamin* *B12* from serum labeled at low pH, as demonstrated by gel chromatography on Sephadex G-200. Further confirmation was obtained by demonstration of a significant correlation...

... ARBC and the R binder content, quantitated as resistance to precipitation by ammonium sulfate at a 2M concentration. Serum labeled at acid pH failed to *deliver* *vitamin* *B12* to Hela *cells* indicating absence of a "functional" TC II-B12 *complex*. The differing *vitamin* *B12* binding capacities of neutral and acidified material was utilized to fractionate the unsaturated *vitamin* *B12*-binding proteins of serum and plasma. The ARBC was used to measure the R binder content, and TC II was calculated from the difference between...

... fractionation procedure was performed on 75 sera and showed increased ARBC in patients with myeloproliferative disorders and decreased ARBC in leukopenia. The content of unsaturated *vitamin* *B12*-binding protein was compared in 75 paired samples of serum and plasma collected from EDTA-anticoagulated blood containing sodium fluoride to inhibit release of granulocyte...

...of fluoridated plasma was significantly lower, due to decreased in vitro R binder release. Plasma also contained less TC II, possibly related to in vitro *cellular* uptake of this binder in fluoridated plasma.

8/3,K/7 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

119278781 CA: 119(26)278781n PATENT

Gene therapy using the intestine

INVENTOR(AUTHOR): Henning, Susan June; Ledley, Fred D.

LOCATION: USA

ASSIGNEE: Baylor College of Medicine

PATENT: PCT International ; WO 9319660 A1 DATE: 931014

APPLICATION: WO 93US3113 (930402) *US 862882 (920403)

PAGES: 44 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61B-001/00A; A61B-010/00B; A61B-017/32B; A61M-031/00B; A61M-035/00B; A61M-039/00B; C12N-015/00B; C12N-015/12B DESIGNATED COUNTRIES: AT; AU; BB; BG; BR; CA; CH; DE; DK; ES; FI; GB; HU; JP; KP; KR; LK; LU; MG; MN; MW; NL; NO; PL; RO; RU; SD; SE; UA DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE ; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

8/3,K/8 (Item 1 from file: 50)

DIALOG(R)File 50:CAB Abstracts

03642098 CAB Accession Numbe[redacted]981417779

Vitamin B12 and B12-proteins. Lectures presented at the 4th European Symposium on Vitamin B12 and B12-Proteins.

Institut fur Organische Chemie, Universitat Innsbruck, Innrain 52a, 6020 Innsbruck, Austria.

Conference Title: Vitamin B12 and B12-proteins. Lectures presented at the 4th European Symposium on Vitamin B12 and B12-Proteins.

xvii + 542 pp.

Publication Year: 1998

Editors: Krautler, B.; Arigoni, D.; Golding, B. T.

Publisher: Wiley-VCH Verlagsgesellschaft mbH -- Weinheim, Germany

ISBN: 3-527-29480-5

Language: English

Document Type: Conference proceedings; Book

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This volume reviews much of the current activities in the *vitamin* *B12*-field, as covered in the lectures *delivered* at the 4th European Symposium on *Vitamin* *B12* and B12-Proteins, which was held at Innsbruck, Austria in September 1996. Individual papers include: B12 coenzymes, the central theme; B12-biosynthesis in an aerobic organism-how the pathway was elucidated; *Vitamin* *B12* biosynthesis in Pseudomonas denitrificans; How nature synthesizes B12 without oxygen-discoveries along the ancient, anaerobic pathway; The biosynthesis of *vitamin* *B12* -assembly of the tetrapyrrole ring system; Investigations on the biosynthesis of the 5,6-dimethylbenzimidazole moiety of *vitamin* *B12*; Cobalamin-dependent methionine synthase from Escherichia coli-structure and reactivity; EPR spectroscopic evidence that in the energy conserving methyltransferase *complex* from methanogenic archaea a histidine residue is ligated to the cobamide-cobalt; Discovery of a biological organometallic reaction sequence involving *vitamin* *B12* ; Corrinoid-dependent methyl transfer reactions in Sporomusa ovata; Spectroscopic and molecular genetic characterization of the two mammalian B12-dependent enzymes; A mechanistic overview of B12...

... mans adenosylcobalamin in the reaction of lysine 2,3-aminomutase; New structural and biosynthetic aspects of the unusual core lipids from Archaebacteria; Cobalamin binding proteins; *Cellular* surface receptors important for *vitamin* *B12* nutrition; The intrinsic factor-cobalamin receptor expressed by yolk sac and proximal tubule epithelial *cells* is the target of teratogenic antibodies; The synthesis and biological activity of radiolabelled cobalamin-diethylenetriaminepentaacetate *complexes*; and B12-nomenclature and a suggested atom-numbering.

8/3,K/9 (Item 1 from file: 442)

00041778

Amyotrophic Lateral Sclerosis; Recent Advances in Pathogenesis and Therapeutic Trials (NEUROLOGICAL REVIEW)

MITSUMOTO, HIROSHI; HANSON, MAURICE R.; CHAD, DAVID A.

Archives of Neurology
February, 1988; 45: 189-2021988;
LINE COUNT: 00728 WORD COUNT: 10047

...Ref. 43,44)

Dementia has been known to occur in certain subsets of ALS, including familial ALS and a form of ALS-parkinsonism-dementia (PD) *complex* found in Guam, the Kii peninsula of Japan, and eastern New Guinea. (Ref. 45-47) Dementia also occurs in otherwise typical ALS. (Ref. 48,49...in other endemic areas, caused a syndrome in primates that clinically and pathologically resembled MND. Whether this plant seed is the cause of

ALS/PD *complex* and whether it has any causal implication to sporadic ALS remains to be clarified. Furthermore, studies among Chamorro migrants from Guam and non-Chamorro migrants...
...tribes with genetically different backgrounds who live on the same small river drainage area were found to have a high incidence of a similar disease *complex*. Environmental factors such as the elemental composition of water and soil where these isolated people live are similar to those found on Guam. (Ref. 106...City, oral communication, November 1986).

Calcium Metabolism

Abnormal calcium metabolism has been suspected not only in sporadic ALS but also in the Guamanian ALS/PD *complex*. (Ref. 201,202) The calcium content of red blood cells from patients with ALS is normal (Ref. 203); muscle calcium levels are decreased, while calmodulin...are present in the sporadic disease. (Ref. 219) Levels of IgG and IgA are found to be increased in Guamanian ALS, (Ref. 220) and immune *complexes* are occasionally found in kidneys of patients with ALS. (Ref. 219) Some investigators have shown the proportion of T-cell lymphocytes reactive to Ia antigen to be increased, (Ref. 202) whereas others have not been able to show such an increase. (Ref. 221) Circulating immune *complex* levels have been found to be elevated in ALS. (Ref. 221,222) Deposits of IgG, C3, and C4 are demonstrated by direct immunofluorescent techniques in...

... or etiologic significance. Serum antibody against neurofilament protein has been found in various degenerative neurologic diseases, most frequently in subacute spongiform encephalopathy, ALS, and PD *complex* . (Ref. 239,240) However, this antibody is now found frequently in healthy individuals, suggesting that the antibody against neurofilament protein may have no pathogenetic significance...and manganese and a low concentration of calcium and magnesium in the soil and water in areas with a high incidence of ALS and PD *complex*. (Ref. 275) Further environmental studies (Ref. 106,107,113) and mineral metabolism analysis (Ref. 202,273) seemed to indicate that an unusual environment could alter...

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